Simulated brain networks reflecting severity of Parkinson's disease

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Introduction

- Parkinson's disease (PD) **progression affects brain networks**, altering their connectivity and topological properties.
- Graph-theoretical measures of the human connectome can be used to reveal **differences in brain networks** between PD patients and healthy individuals[1].
- Dynamical brain models allow us for a detailed investigation of brain dynamics ***in silico***, providing deep insights into progression of the neurodegenerative diseases and treatment effects.
- Whole-brain models demonstrate that **simulated brain networks significantly correlate with clinical measures**, potentially offering a new biomarker for disease progression.

Methods: Whole-brain dynamical modeling based on network properties

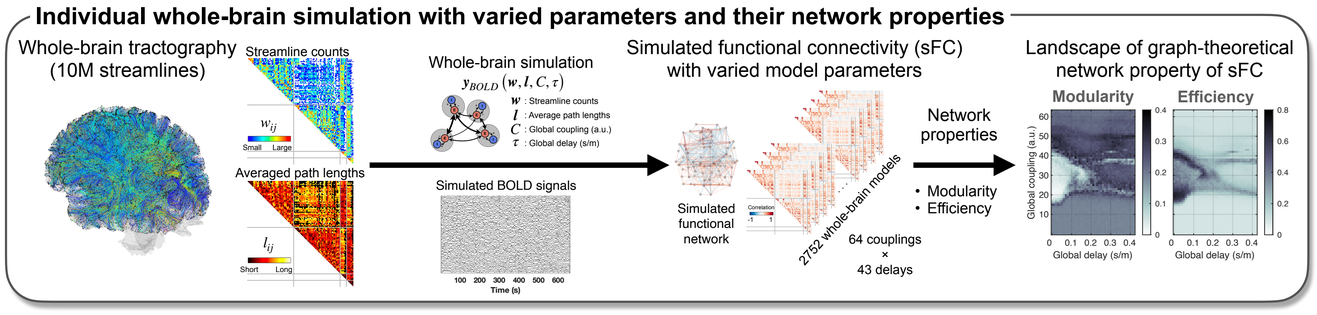
❖ **Participants: 51** (30 males) **healthy controls** and **60** (43 males) **patients** with Parkinson's disease.
- MRI acquisition: T1-weighted image, resting-state fMRI (rsfMRI), and diffusion-weighted images (DWI) with 64 directions.
- MRI processing: Extracting blood oxygenation level-dependent (BOLD) signals from rsfMRI and reconstructing whole-brain tractography with 10M streamlines using DWI.
- Two parcellation schemes: Schaefer 100 Parcels and Desikan-Killiany including subcortical areas.

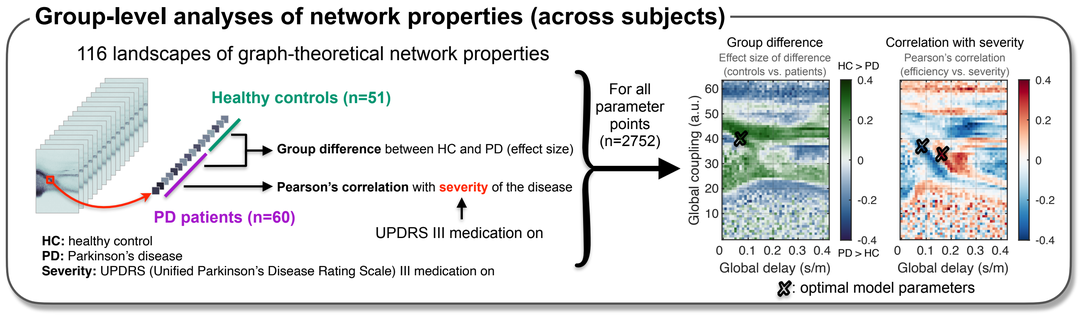
❖ **Whole-brain model:** Biophysical two-population model (reduced Jansen-Rit type[2-4]) for electrical signals + Balloon-Windkessel model[5,6] for BOLD signals.

❖ **Network-based behavioral model fitting:** **Modularity** and **global efficiency** of simulated brain networks opted for **group differentiation** and **relationship with severity of the disease**.

MRI pipeline

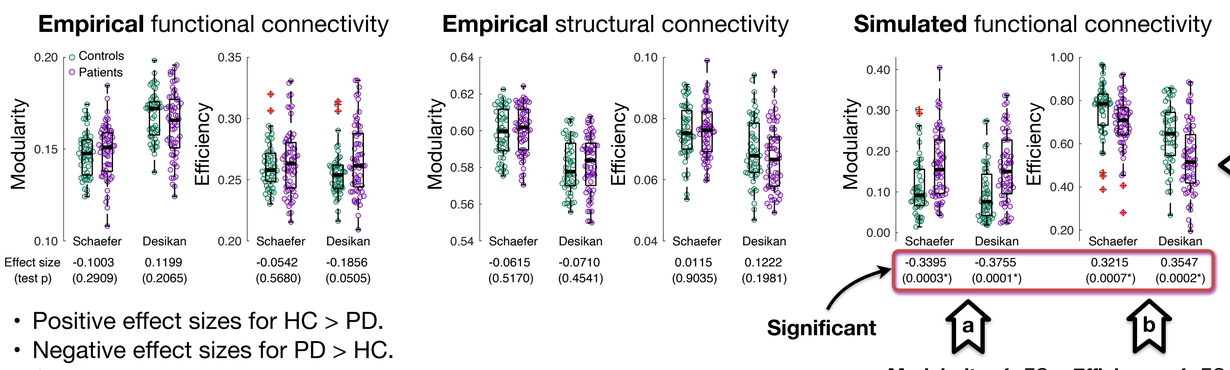
Preprint





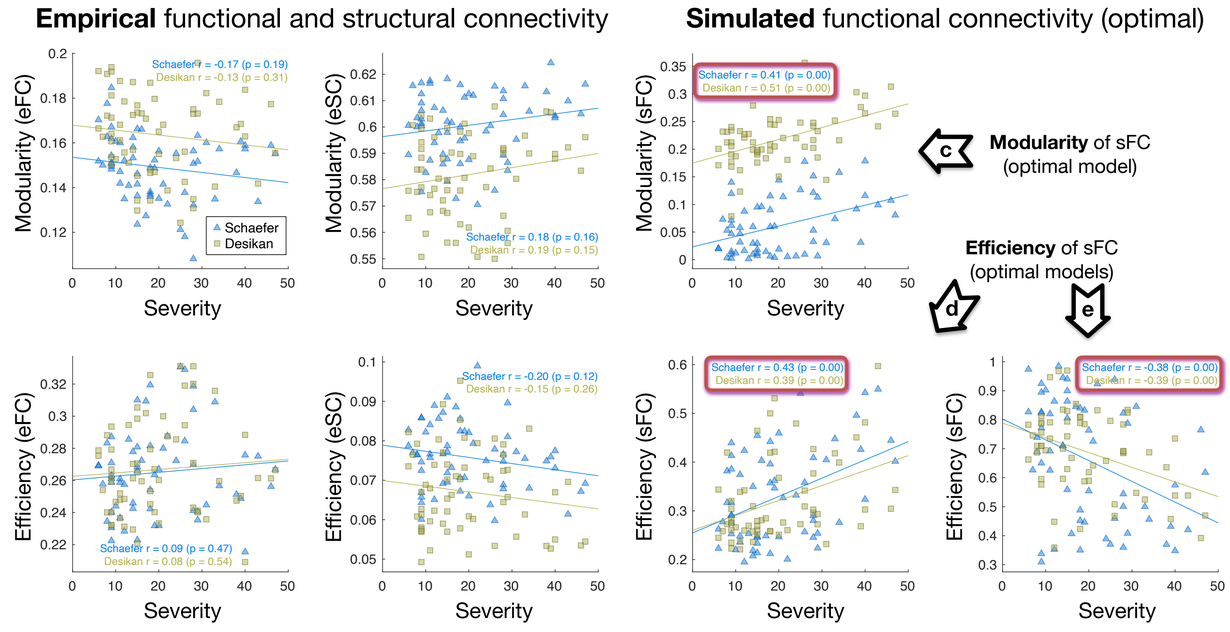
Results: Simulated brain networks outperforming empirical brain networks in clinical analyses

1. Group differences in network properties bewteen controls and patients.



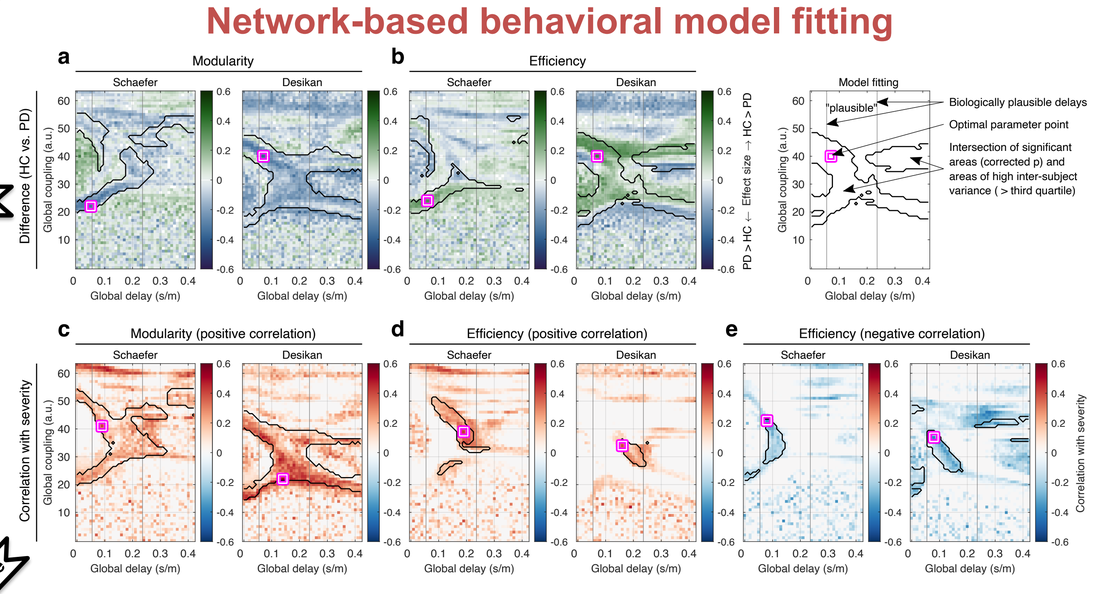
- Positive effect sizes for HC > PD.
- Negative effect sizes for PD > HC.
- Statistics *p*-values of the Wilcoxon rank-sum two-tail test.
- Simulated FC derived by optimal models with optimal parameters described in the **Network-based behavioral model fitting (a and b)**.

2. Correlations between network properties and severity of the disease.



- **Severity**: UPDRS III medication on.
- Pearson's correlation coefficient (*p*-value) for each parcellation condition.
- Simulated FC calculated by optimal models with optimal parameters described in the **Network-based behavioral model fitting (c, d, and e)**.

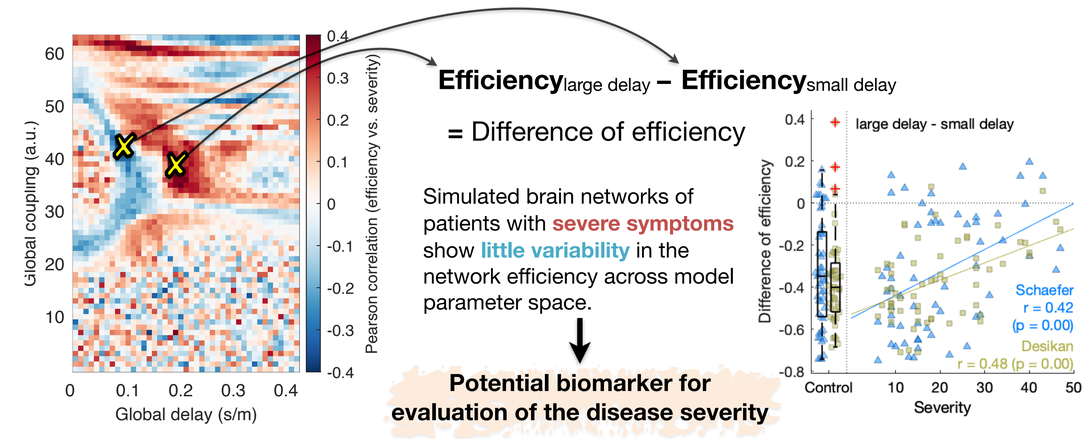
Network-based behavioral model fitting



(a-b) Landscapes of the effect size of the group difference between healthy controls (HC) and patients with Parkinson's disease (PD). Optimal parameter points of the largest effect sizes.
(c-e) Landscapes of Pearson's correlation (across PD patients) between simulated network properties and severity (UPDRS III medication on). Optimal parameter points of the strongest correlations.

Black contour curves (optimal parameters were selected in the contour areas)
➡Significant areas using the random-field theory **AND** Areas of high inter-subject variance (> third quartile).

3. Network alteration in optimal models relates to the severity.



Conclusion

- **Simulated brain networks** of the whole-brain dynamical models can be utilized for demonstrating **relationships** between brain dynamics and **clinical measures**.
- **Network-based behavioral model fitting** **enhances differentiation** of disease and control groups and results in **significant relationships** between simulated network properties and severity of the disease.
- Modeling results can **outperform empirical data** and can be a **potential biomarker** applied for objective evaluations of the disease severity and progression.

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